

25(112), June, 2021

Post covid hypothalamic-pituitary-adrenal axis dysfunction manifesting as perinatal depression: A case series

To Cite:

Talwar D, Madaan S, Kumar S, Jaiswal A, Khanna S, Hulkoti V, Eleti MR. Post covid hypothalamic-pituitary-adrenal axis dysfunction manifesting as perinatal depression: A case series. *Medical Science*, 2021, 25(112), 1402-1406

Author Affiliation:

¹Post Graduate Resident, Department of Medicine , Jawaharlal Nehru medical college, Datta Meghe Institute of Medical Sciences (Deemed to be University), Wardha, Maharashtra, India

²Post Graduate Resident, Department of Obstetrics and Gynaecology, Jawaharlal Nehru medical college, Datta Meghe Institute of Medical Sciences (Deemed to be University), Wardha, Maharashtra, India

³Professor, Department of Medicine, Jawaharlal Nehru medical college, Datta Meghe Institute of Medical Sciences (Deemed to be University), Wardha, Maharashtra, India

⁴Professor, Department of Obstetrics and Gynaecology, Jawaharlal Nehru medical college, Datta Meghe Institute of Medical Sciences (Deemed to be University), Wardha, Maharashtra, India

✉ Corresponding author

Post Graduate Resident, Department of Obstetrics and Gynaecology, Jawaharlal Nehru medical college, Datta Meghe Institute of Medical Sciences (Deemed to be University), Wardha, Maharashtra, India

Email: sparsh19madaan@gmail.com

Peer-Review History

Received: 08 May 2021

Reviewed & Revised: 09/May/2021 to 05/June/2021

Accepted: 06 June 2021

Published: June 2021

Peer-review Method

External peer-review was done through double-blind method.

Dhruv Talwar¹, Sparsh Madaan^{2✉}, Sunil Kumar³, Arpita Jaiswal⁴, Shivam Khanna¹, Vidyashree Hulkoti¹, Manila Reddy Eleti²

ABSTRACT

Since 2019, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS CoV2) has led to major impact on both the physical as well as mental health. Although the health care facilities aim to provide treatment for the respiratory, cardiovascular as well as neurological manifestations, its huge impact on the mental wellness of patients is somewhat neglected. Perinatal depression is a commonly encountered psychological disorder. Various factors can aggravate or trigger post-partum depression. COVID-19 is one of such triggers. There is microglial cell activation leading to neuroinflammation along with Hypothalmo-pituitary Axis Dysfunction in COVID-19 leading to neuropsychiatric manifestations. Also similarity in genes for Angiotensin Convertase Enzyme 2 and Dopa Decarboxylase leads to reduction in Dopamine and Serotonin in COVID-19 patients leading to Depression. While complications like HELLP Syndrome and Intra Uterine Death remain well reported in association with COVID-19, Post-Partum Depression remains an underreported post COVID sequelae. Thus, we report a case series of COVID-19 positive pregnant patients who suffered from postpartum depression later as a Post COVID sequelae and were successfully treated with antidepressants and cognitive behavioral therapy preventing any complications.

Keywords: COVID-19, Perinatal depression, Hypothalmo-pituitary-adrenal axis

1. INTRODUCTION

Since December 2019, there has been a rapid spread of novel coronavirus (COVID-19) worldwide. The stress of the ongoing pandemic is distressing with increasing mortality, morbidity, uncertainty as well as strained health care facilities (Wanjari et al., 2020). Due to ongoing strain to the healthcare system the social as well as psychological effect exerted by COVID-19 has

taken a backseat. There has been isolation from social interactions further disabling patients from getting comfort in the form of human interactions. There is a growing need to address the psychological impact of COVID-19 to prevent serious complications in the future. It has been seen in the past that outbreak of infectious diseases increases the amount of anxiety and depression. Pregnancy is a vulnerable state where COVID-19 can impact both the patient as well as the fetus. Also, in the outbreak of infectious diseases the incidence of depression is more in females therefore Pregnant COVID-19 patients are much more vulnerable to develop depression. It is essential to treat ante natal and post-partum psychiatric complications during virus outbreaks as it was reported that the psychiatric complications seen in ante natal females in the previous outbreaks of infectious diseases led to higher incidence of psychiatric illness in the children born (Felder et al., 2020). It has been postulated that the cytokine storm associated with COVID-19 has a major role in neuropsychiatric manifestations of COVID-19.

A increased amount of inflammatory markers were also detected in patients developing complications like psychosis, depression as well as post-traumatic stress disorder thus further supporting the role of cytokine storm in neuropsychiatric manifestations of COVID-19. Biochemical alterations are also a possible cause of neuropsychiatric manifestations of COVID-19 with reduced amount of Serotonin and Dopamine detected in COVID-19. While COVID-19 has a long list of manifestations a prolonged inflammation even after cure. There is microglial cell activation leading to extensive neuroinflammation and depression along with anxiety.

sequalae following up to a period of 3 months after COVID-19 are known as Post COVID sequalae. While the consequences of the emotional and mental well-being on the Survivors of COVID-19 who enter the Post COVID sequalae has not been documented, it is predicted that mental health disorders will emerge as an alarming emergency in the near future. Furthermore, its impact on pregnancy is even more dangerous given the high risk associated with pregnancy as well as increased vulnerability of pregnant females to develop neuropsychiatric manifestations as a Post COVID sequalae (Lebel et al., 2021). Immunological aberration as well exaggerated inflammatory damage caused by the SARS Cov 2 might be the reason for wide range of Post COVID manifestations. We Report a case series of pregnant females who contracted COVID-19 and alter on presented with Perinatal Depression.

2. CASE SERIES

Case 1

A 23-year-old patient who had delivered her first child one month ago presented with the chief complaint of lack of concentration as well as awareness, sleeping disturbances, loss of appetite and pessimistic vision of the future. Patient had history of COVID-19 a month ago when she was tested by RTPCR method before her delivery. Her Post partum HRCT showed bilateral ground glass opacities with CT Severity score of 5/25 and CORAD 6 (figure 1). Patient was kept quarantined for 14 days and hence was unable to be with her child for the duration of 14 days after birth. There was no history of any psychiatric illness in the past. Her general examination showed pulse 74 beats per minute, regular in rhythm, blood pressure 130/82 mm hg in right arm supine posture and spo₂ was 96 on room air. Systemic examination revealed conscious and oriented patient with normal deep tendon and superficial reflexes and Motor function was also normal. Edinburgh Post Natal Depression Scale was used to establish a diagnosis of Postpartum Depression and she scored 19 on the EPDS test. Rest of the systemic examination was unremarkable. The patient was admitted and lab investigations revealed raised inflammatory markers with a normal thyroid profile (table 1). She was started on supportive therapy as well as cognitive behavioural therapy, Short serotonin reuptake inhibitors and was continued on steroids in view of increased inflammatory markers. The patient improved clinically and was discharged after one week in stable condition. She is doing well on follow up.



Figure 1 Showing HRCT Thorax of Case 1 with bilateral Ground Glass opacity

Case 2

A 29 year old patient who delivered her second child one month and 8 days back presented with the complaint of loss of interest, fatigue, loss of confidence as well as self awareness and persistent thoughts of worthlessness and guilt. She also had constant worry about her child's well being. Patient had history of COVID-19 infection a month ago following her delivery when her HRCT showed. Bilateral ground glass opacities with a CT severity score of 17/25 and CORAD 6 (figure 2). There was no history of any psychiatric illness in the past and previous delivery was conducted 2 years back with no evidence of post partum blue or depression .On general examination pulse was 84 beats per minutre, regular, blood pressure was 120/76 mm hg in right arm supine position and spo₂ was 97 on room air. Systemic examination showed patient to be conscious, oriented, all deep tendon and superficial reflexes were normal, sensory and motor functions were intact .Edinburgh Post Natal Depression Scale was used to establish a diagnosis of Postpartum Depression and she scored 20 on the EPDS test. Patient was admitted and lab investigations showed normal thyroid function with raised inflammatory markers (table 1). Patient was started on cognitive behavioural therapy and was continued on corticosteroids in view of increased inflammatory markers. She was discharged eight days after admission after clinical improvement.



Figure 2 HRCT Thorax of Case 2 Showing bilateral ground glass opacity

Table 1 Showing lab investigations of both the cases

Lab Paramteter	Case 1 AGE-23 Years SEX-FEMALE	Case 2 AGE-29 Years SEX-FEMALE
CBC	Hb-11.5gm/dl MCV-88fl Platelet count-112000/dl WBC Count-7700/dl	Hb10.9gm/dl, MCV:89fl, Platelet count 113000/dl, WBC Count 8900/dl
LFT	Total Protein-6.8gm/dl, Albumin3.4gm/dl, Globulin3.4gm/dl, aspartate aminotransferase 23 units/l , alanine aminotransferase 27 units/l, Alkanline Phophatase 94IU/l, Total Bilirubin :1.13mg/	Total Protein-6.5gm/dl, Albumin3.2gm/dl, Globulin3.3gm/dl, aspartate aminotransferase 21 units/l , alanine aminotransferase 31 units/l ,Alkanline Phophatase 101 IU/l, Total Bilirubin :1.19mg
KFT	Creatinine:1.4mg/dl, Urea31mg/dl, Sodium137mmol/l,	Creatinine:1.1mg/dl, Urea38mg/dl, Sodium 135mmol/l,

	Potassium -4.7mmol/l	Potassium – 3.7 mmol/l
CRP	42.0mg/dl	51.7mg/dl
D-Dimer	0.78	0.72
Serum Ferritin	550ng/ml	620ng/ml
Thyroid Profile	TSH-0.43 Free T3-320 pg/ml Free T4-1.1ng/dl	TSH-2.2 Free T3-300 pg/ml Free T4-0.98ng/dl
HRCT Score	5/25	17/25
CORAD	6	6

3. DISCUSSION

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS CoV 2) has caused an emergence of varied presentations. It may range from a mild upper respiratory tract infection to acute respiratory distress syndrome (Jain et al., 2020). Although the presentations like Respiratory Distress, Myocardial Infarction and Stroke have been given much importance, neuropsychiatric manifestations seem to have been neglected worldwide. It is important to note that SARS CoV2 modulates the expression of angiotensin convertase enzyme 2 and the expression of ACE 2 is seen not only in the lung but also in the hypothalamus, adrenal and pituitary. This leads to a dysfunction of the hypothalamo-pituitary-adrenal axis further leading to Neuropsychiatric manifestations like depression in our case. Also, Inflammatory Cytokines released in COVID-19 induce the action of microglial cells thus leading to profound neuroinflammation (Talwar et al., 2021). The above mentioned pathophysiology of depression in COVID-19 is further synergised by Stress due to the trying ongoing pandemic. It is also important to note that case 1, was unable to meet her new born child for duration of 14 days and that might have further exacerbated the depression and anxiety. During the perinatal period, patients also tend to have more anxiety about the wellbeing of neonate (Tomfohr-Madsen et al., 2021). Thus, the above factors form a synergistic effect predisposing a female in perinatal period to experience depression (Figure 3).

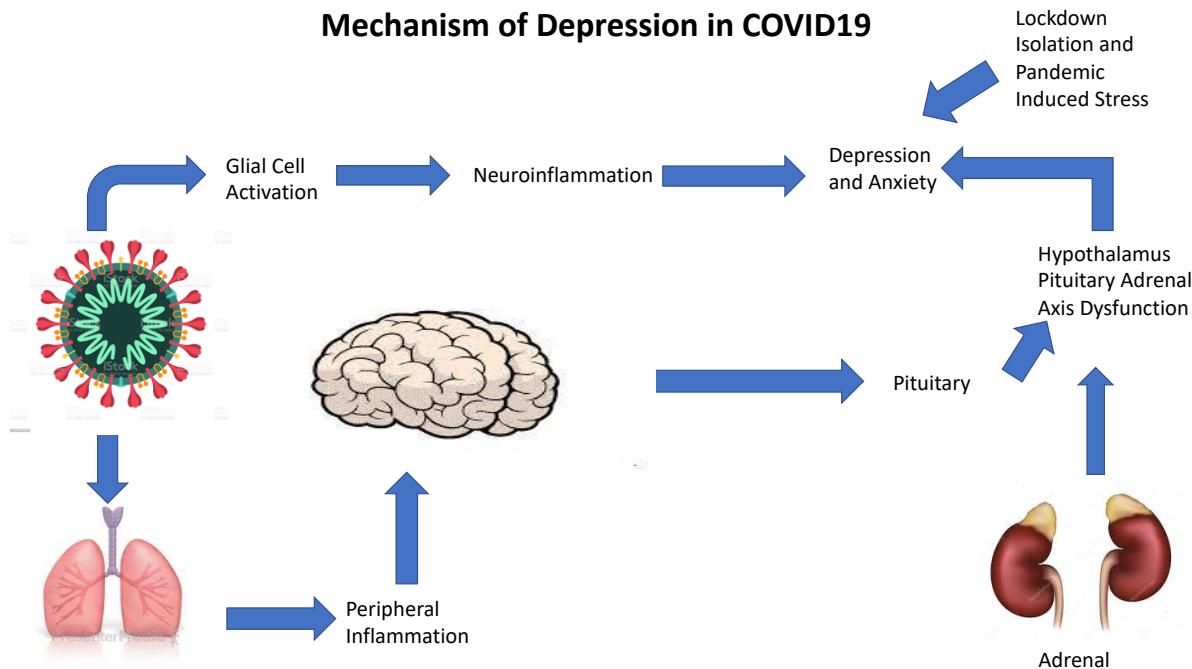


Figure 3 Pathophysiology of Depression linked with COVID-19

It is important to note that the female of case 1 was just treated with behavioural therapy and corticosteroids thus supporting the role of HPA Axis dysfunction, neuroinflammation and inflammatory cytokine induced microglial activity in her depression. In the presence of above scenario, it is reasonable to conclude that COVID-19 induced inflammation and HPA Axis dysfunction had the key role in perinatal depression seen in our case series.

4. CONCLUSION

We present a case series of two patients who presented with Perinatal Depression as a sequela of Post COVID which otherwise is a neglected outcome of COVID-19 in pregnancy. We highlight that COVID-19 may manifest as hypothalmo-pituitary-adrenal axis dysfunction leading on to cause depression. Thus, the clinicians treating COVID-19 should be on the lookout of HPA Axis dysfunction to mitigate neuropsychiatric manifestations and further complications in Post COVID period.

Acknowledgement

We thank all the participants who have contributed in this Study.

Conflict of interest

The Authors have no conflicts of interest that are directly relevant to the content of this clinic-pathological case.

Financial Resources

There are no financial resources to fund this study

Informed Consent

Informed Consent was obtained from the patient.

Author's Contribution

All the authors contributed equally to the case report.

Data and materials availability

All data associated with this study are present in the paper.

REFERENCES AND NOTES

1. Felder JN, Epel ES, Neuhaus J, Krystal AD, Prather AA. Efficacy of Digital Cognitive Behavioral Therapy for the Treatment of Insomnia Symptoms among Pregnant Women: A Randomized Clinical Trial. *JAMA Psychiatry* 2020; 77(5):484-492.
2. Jain A, Talwar D, Kumar S. Spectrum of Respiratory Involvement in COVID 19 Era; An Overview. *Indian J of Forensic Med & Toxicol* 2020; 14(4):6593-9.
3. Lebel C, MacKinnon A, Bagshawe M, Tomfohr-Madsen L, Giesbrecht G. Elevated depression and anxiety symptoms among pregnant individuals during the COVID-19 pandemic. *J Affect Disord* 2020; 277:5-13.
4. Talwar D, Kumar S, Madaan S, Khanna S, Annadatha A. Intractable Singultus: Atypical presentation of COVID 19. *Medical Science* 2021; 25(111), 1183-1187
5. Tomfohr-Madsen LM, Racine N, Giesbrecht GF, Lebel C, Madigan S. Depression and anxiety in pregnancy during COVID-19: A rapid review and meta-analysis. *Psychiatry Res* 2021; 300:113912
6. Wanjari AK, Ayush Dubey, Sourav Chaturvedi, Sunil Kumar. Young COVID 19 presenting as fatal subarachnoid hemorrhage: Association or chance?. *Medical Science* 2020; 24(104), 2712-2715